amino acid thus reducing the reactivity with a panel of murine monoclonal antibodies provided that the other amino acid is not alanine.

32. (New) Staphylokinase derivatives as claimed in claim 31 having essentially the amino acid sequence as depicted in figure 1 in which one or more amino acids have been replaced by another amino acid thus reducing the absorption of SakSTAR-specific antibodies from plasma of patients treated with staphylokinase provided that the other amino acid is not alanine.

33. (New) Staphylokinase derivatives as claimed in claim 31 having essentially the amino acid sequence as depicted in figure 1 in which one or more amino acids have been replaced by other amino acids, without reducing the specific activity by more than 50 percent provided that the other amino acid is not alanine.

34. (New) Staphylokinase derivatives SakSTAR (K35X, G36X, E65X, K74X, E80X, D82X, K102X, E108X, K109X, K121X, K130X, K135X, K136X, +137X) having the amino acid sequence as depicted in figure 1 in which one or more of the amino acids Lys in position 35, Gly in position 36, Glu in position 65, Lys in position 74, Glu in position 80, Asp in position 82, Lys in position 102, Glu in position 108, Lys in position 109, Lys in position 121, Lys in position 130, Lys in position 135 and/or Lys in position 136 have been replaced with other amino acids provided that the other amino acid is not alanine and/or in which one amino acid has been added at the COOH-terminus, thus altering the immunogenicity after administration in patients, without markedly reducing the specific activity.

35. (New) Staphylokinase derivatives listed in Tables 1, 3, 4, 5, 6, 7, 8, 13, 19 and 20, having the amino acid sequence as depicted in figure 1 in which the indicated amino acids have been replaced by other amino acids thus reducing the absorption of SakSTAR-specific antibodies from plasma of patients treated with staphylokinase, without reducing the specific activity, provided that at least one amino acid is replaced with an amino acid other than alanine.

36. (New) Staphylokinase derivative as claimed in claim 31, selected from the group consisting of SakSTAR (S34G, G36R, H43R), SakSTAR (S34G, G36R, H43R), SakSTAR (G36R), SakSTAR (H43R), SakSTAR (G36R, K74R), SakSTAR (K35E), SakSTAR (K74Q), SakSTAR (K130T), SakSTAR (V132L), SakSTAR (V132T), SakSTAR (V132N), SakSTAR (V132R), SakSTAR (K130T, K135R), SakSTAR (G36R, K130T, K135R), SakSTAR (K74R, K130T, K135R), SakSTAR (K74Q, K130T, K135R), SakSTAR (G36R, K74R, K130T, K135R), SakSTAR (G36R, K74Q, K130T, K135R), SakSTAR (G36R, H43R, K74R, K130T, K135R), SakSTAR (E65A, K74Q, K130T, K135R), SakSTAR (E65Q, K74Q, K130T, K135R), SakSTAR (K74Q, K86A, K130T, K135R), SakSTAR (E65Q, T71S, K74Q, K130T, K135R), SakSTAR (K74Q, K130A, K135R), SakSTAR (E65Q, K74Q, K130A, K135R), SakSTAR (K74Q, K130E, K135R), SakSTAR (K74Q, K130E, V132R, K135R), SakSTAR (E65Q, K74Q, T90A, K130A, K135R), SakSTAR (E65Q, K74Q, N95A, K130A, K135R), SakSTAR (E65Q, K74Q, E118A, K130A, K135R), SakSTAR (E65Q, K74Q, N95A, E118A, K130A, K135R), SakSTAR (N95A, K130A, K135R), SakSTAR (E65Q, K74Q, K109A, K130T, K135R), SakSTAR (E65Q, K74Q, E108A, K109A, K130T, K135R), SakSTAR (E65Q, K74Q, K121A, K130T, K135R), SakSTAR (E65Q, K74Q, N95A, E118A, K130A, K135R, K136A, +137K), SakSTAR (E80A, D82A, K130T, K135R), SakSTAR (K74R, E80A, D82A, K130T, K135R), SakSTAR (K74Q, E80A, D82A, K130T, K135R), SakSTAR (K35A, K74R, E80A, D82A, K130T, K135R), SakSTAR

(E65D, K74R, E80A, D82A, K130T, K135R), SakSTAR (E65S, K74R, E80A, D82A, K130T, K135R), SakSTAR (S34G, G36R, K74R, K130T, K135R), SakSTAR (E65A, K74R, E80A, D82A, K130T, K135R), SakSTAR (E65N, K74R, E80A, D82A, K130T, K135R), SakSTAR (E65Q, K74R, E80A, D82A, K130T, K135R), SakSTAR (K57A, E58A, E61A, E80A, D82A, K130T, K135R), SakSTAR (E65D, K74Q, E80A, D82A, K130T, K135R), SakSTAR (E65Q, K74Q, E80A, D82A, K130T, K135R), SakSTAR (K35A, E65D, K74Q, E80A, D82A, K130T, K135R), SakSTAR (K74R, E80A, D82A, S103A, K130T, K135R), SakSTAR (E65D, K74R, E80A, D82A, K109A, K130T, K135R), SakSTAR (E65D, K74R, E80A, D82A, K130T, K135R, K136A), SakSTAR (E65Q, K74Q, D82A, S84A, K130T, K135R), SakSTAR (K35A, K74Q, E80A, D82A, K130T, K135R), and SakSTAR (K35A, E65D, K74R, E80A, D82A, K130T, K135R).

37. (New) SakSTAR (E65D, K74R, E80A, D82A, K130T, K135R) having the code SY19.

38. (New) SakSTAR (K35A, E65Q, K74R, E80A, D82A, T90A, E99D, T101S, E108A, K109A, K130T, K135R) having the code SY161.

39. (New) Staphylokinase derivatives having essentially the amino acid sequence as depicted in figure 1 in which one or more amino acids have been replaced by another amino acid thus reducing the reactivity with a panel of murine monoclonal antibodies and having in addition either one or both of the following:

at least one amino acid substituted with Cys, resulting in dimerization and/or increased specific activity and/or reduced clearance and/or increased thrombolytic potency; and/or

polyethylene glycol substitution, resulting in a significantly reduced plasma clearance while maintaining specific activity.

40. (New) Staphylokinase derivatives as claimed in claim 39 having essentially the amino acid sequence as depicted in figure 1 in which one or more amino acids have been replaced by another amino acid thus reducing the absorption of SakSTAR-specific antibodies from plasma of patients treated with staphylokinase.

41. (New) Staphylokinase derivatives as claimed in claim 39 having essentially the amino acid sequence as depicted in figure 1 in which one or more amino acids have been replaced by other amino acids, without reducing the specific activity by more than 50 percent.

42. (New) Staphyokinase derivatives as claimed in claim 39, named SakSTAR (K35X, G36X, E65X, K74X, E80X, D82X, K102X, E108X, K109X, K121X, K130X, K135X, K136X, +137X) and having the amino acid sequence as depicted in figure 1 in which one or more of the amino acids Lys in position 35, Gly in position 36, Glu in position 65, Lys in position 74, Glu in position 80, Asp in position 82, Lys in position 102, Glu in position 108, Lys in position 109, Lys in position 121, Lys in position 130, Lys in position 135 and/or Lys in position 136 have been replaced with other amino acids and/or in which one amino acid has been added at the COOH-terminus, thus altering the immunogenicity after administration in patients, without markedly reducing the specific activity.

43. (New) Staphylokinase derivatives as claimed in claim 39 and listed in Tables 1, 3, 4, 5, 6, 7, 8, 13, 19 and 20, having the amino acid sequence as depicted in figure 1 in which the indicated amino acids have been replaced by ther amino acids thus reducing the absorption of SakSTAR-specific antibodies from plasma of patients treated with staphylokinase, without reducing the specific activity.

44. (New) Staphylokinase derivative as claimed in claim 39, selected from the group consisting of SakSTAR (K74A, E75A, R77A), SakSTAR (K35A, E75A), SakSTAR (E75A), SakSTAR (E80A, D82A), SakSTAR (E80A), SakSTAR (D82A), SakSTAR (E75A, D82A), SakSTAR (S34G, G36R, H43R), SakSTAR (K35A), SakSTAR (D82A), SakSTAR (D82A, S84A), SakSTAR (T90A), SakSTAR (Y92A), SakSTAR (K130A), SakSTAR (V132A), SakSTAR (S34G, G36R, H43R), SakSTAR (G36R), SakSTAR (H43R), SakSTAR (G36R, K74R), SakSTAR (K35E), SakSTAR (K74Q), SakSTAR (K130T), SakSTAR (V132L), SakSTAR (V132T), SakSTAR (V132N), SakSTAR (V132R), SakSTAR (K130T, K135R), SakSTAR (G36R, K130T, K135R), SakSTAR (K74R, K130T, K135R), SakSTAR (K74Q, K130T, K135R), SakSTAR (G36R, K74R, K130T, K135R), SakSTAR (G36R, K74Q, K130T, K135R), SakSTAR (G36R, H43R, K74R, K130T, K135R), SakSTAR (E65A, K74Q, K130T, K135R), SakSTAR (E65Q, K74Q, K130T, K135R), SakSTAR (K74Q, K86A, K130T, K135R), SakSTAR (E65Q, T71S, K74Q, K130T, K135R), SakSTAR (K74Q, K130A, K135R), SakSTAR (E65Q, K74Q, K130A, K135R), SakSTAR (K74Q, K130E, K135R), SakSTAR (K74Q, K130E, V132R, K135R), SakSTAR (E65Q, K74Q, T90A, K130A, K135R), SakSTAR (E65Q, K74Q, N95A, K130A, K135R), SakSTAR (E65Q, K74Q, E118A, K130A, K135R), SakSTAR (E65Q, K74Q, N95A, E118A, K130A, K135R), SakSTAR (N95A, K130A, K135R), SakSTAR (E65Q, K74Q, K109A, K130T, K135R), SakSTAR (E65Q, K74Q, E108A, K109A, K130T, K135R),

SakSTAR (E65Q, K74Q, K121A, K130T, K135R), SakSTAR (E65Q, K74Q, N95A, E118A, K130A, K135R, K136A, +137K), SakSTAR (E80A, D82A, K130T, K135R), SakSTAR (K74R, E80A, D82A, K130T, K135R), SakSTAR (K74Q, E80A, D82A, K130T, K135R), SakSTAR (K35A, K74R, E80A, D82A, K130T, K135R), SakSTAR (E65D, K74R, E80A, D82A, K130T, K135R), SakSTAR (E65S, K74R, E80A, D82A, K130T, K135R), SakSTAR (S34G, G36R, K74R, K130T, K135R), SakSTAR (E65A, K74R, E80A, D82A, K130T, K135R), SakSTAR (E65N, K74R, E80A, D82A, K130T, K135R), SakSTAR (E65Q, K74R, E80A, D82A, K130T, K135R), SakSTAR (K57A, E58A, E61A, E80A, D82A, K130T, K135R), SakSTAR (E65D, K74Q, E80A, D82A, K130T, K135R), SakSTAR (E65Q, K74Q, E80A, D82A, K130T, K135R), SakSTAR (K35A, E65D, K74Q, E80A, D82A, K130T, K135R), SakSTAR (K74R, E80A, D82A, S103A, K130T, K135R), SakSTAR (E65D, K74R, E80A, D82A, K109A, K130T, K135R), SakSTAR (E65D, K74R, E80A, D82A, K130T, K135R, K136A), SakSTAR (E65Q, K74Q, D82A, S84A, K130T, K135R), SakSTAR (K35A, K74Q, E80A, D82A, K130T, K135R), and SakSTAR (K35A, E65D, K74R, E80A, D82A, K130T, K135R).

45. (New) Staphylokinase derivatives as claimed in claim 39, wherein the Cys is chemically modified with polyethylene glycol with molecular weights up to 20 kDa.

46. (New) Staphylokinase derivatives as claimed in claim 45, wherein selected amino acids in the NH_2-terminal region of 10 amino acids, are substituted with Cys, which is chemically modified with polyethylene glycol with molecular weights up to 20 kDa, which derivatives are characterized by a significantly reduced plasma clearance and maintained thrombolytic potency upon single intravenous bolus administration at a reduced dose.

47. (New) Staphylokinase derivative as claimed in claim 46, wherein the serine in position 2 or 3 is substituted with a cystein and the cystein is chemically modified with polyethylene glycol having a molecular weight of 5, 10 or 20 kDa.

48. (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakSTAR (S3C-MP5, K35A, E65Q, K74R, E80A, D82A, T90A, E99D, T101S, E108A, K109A, K130T, K135R) having the code of SY161 (S3C-MP5).

49 (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakSTAR (S3C-P10, K35A, E65Q, K74R, E80A, D82A, T90A, E99D, T101S, E108A, K109A, K130T, K135R) having the code of SY161 (S3C-P10).

50. (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakSTAR (S3C-P20, K35A, E65Q, K74R, E80A, D82A, T90A, E99D, T101S, E108A, K109A, K130T, K135R) having the code of SY161 (S3C-P20).

51. (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakSTAR (S3C-MP5, E65D, K74R, E80A, D82A, K130T, K135R) having the code of SY19 (S3C-MP5).

52. (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakStar(S3C-SP5, E65D, K74R, E80A, D82A, K130T, K135R) having the code of SY19 (S3C-SP5).

53. (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakSTAR (S2C-SP5, S3C-SP5, E65D, K74R, E80A, D82A, K130T, K135R) having the code of SY19 (S2C-SP5, S3C-SP5).

54. (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakSTAR (S3C-P20, E65D, K74R, E80A, D82A, K130T, K135R) having the code of SY19(S3C-P20).

55. (New) Staphylokinase derivative as claimed in claim 47, which derivative is SakSTAR (S3C-P20, E65D, K74R, E80A, D82A, K130T, K135R) having the code of SY19(S3C-P10).

56. (New) Dimer of two staphylokinase derivatives as claimed in claim 39.

57. (New) Method for producing the staphylokinase derivatives as claimed in claim 31, comprising the steps of:

preparing a DNA fragment comprising at least the part of the coding sequence of staphylokinase that provides for its biological activity;

performing *in vitro* site-directed mutagnesis on the DNA fragment to replace one or more codons for wild-type amino acids by a codon for another amino acid;

cloning the mutated DNA fragment in a suitable vector;

transforming or transfecting a suitable host cell with the vector; and

culturing the host cell under conditions suitable for expressing the DNA fragment.

58. (New) Method as claimed in claim 57, wherein the DNA fragment is a 453 bp Eco-RI-HindIII fragment of the plasmid pMEX602sakB, the *in vitro* site-directed mutagenesis is performed and the mutated DNA fragment is expressed in *E. Coli*.

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59. (New) Pharmaceutical composition comprising at least one of the staphylokinase derivatives as claimed in claim 31, together with a suitable excipient.

60. (New) Pharmaceutical composition as claimed in claim 59 for treating arterial thrombosis.